REMARKS

Claims 1, 3, 5-11, 13-15, 36-49, 51, and 60-76 are pending. Claims 1, 3, 14, 15, 36, 38, 39-42, 46-49, and 60-61 are amended and claims 62-76 are new. Claims 3, 5-11, 45-48, and 51 are withdrawn as they are directed to a non-elected species. However, since the requirements of claim 16 to specific polymers that are acid resins have been added to claim 1, the amendment makes the election of species moot. Claim 16 is canceled herein. The amendment to claim 1 is supported by original claim 16 and paragraph [0014] (human subject). The amendment to claim 14 is supported in the specification, for example, at paragraph [0019]. The amendment to claim 15 is to correct a typographical error. The amendments to claims 36, 38-42, and 60-61 are supported, for example, in the specification at paragraph [0014]. The amendment to claim 61 is supported in the specification at paragraph [0072]. New claim 62 is supported, for example, by original claims 1, 16, and 39 and paragraph [0019]. New claim 63 is supported by original claim 9 and new claims 64-71 and 73-76 are supported, for example, by original claims 36-43 and 16, 51, 60, and 61, respectively. New claim 72 is supported, for example, by original claims 1 and 49 and by paragraph [0013].

Examiner Interview

On December 9, 2008, Examiner Neil Levy had a personal interview with Dr. Gerrit Klaerner (inventor), Ronald Krasnow (representing Relypsa Inc.) and Janet S. Hendrickson and Kathleen M. Petrillo (attorneys for Applicants). In the interview, the parties discussed the final rejection mailed on November 12, 2008. Examiner Levy stated that if claim 1 were limited to humans and the polymers of claim 16 were incorporated into claim 1, the outstanding rejections would be overcome.

On May 14, 2009, Examiner Neil Levy had a telephonic interview with Janet S. Hendrickson (attorney for Applicants). In the interview, Ms. Hendrickson stated her expectation that the outstanding rejections would be overcome with the amendments made, but Examiner Levy stated that there were other issues with the claims that still needed resolution. Examiner Levy further stated that the obviousness-type double patenting rejection would be maintained even if the amendments would have been entered.

35 U.S.C. § 112

Reconsideration is requested of the rejection of claim 1, 13-15, 36-44, 60, and 61 as not satisfying the enablement requirement of 35 U.S.C. § 112, first paragraph. While Applicant believes the arguments presented in the response filed on August 20, 2008 are persuasive, to expedite prosecution, claim 1 has been amended in a manner that the Office's prior Office action and interview summary indicated would overcome this rejection. Further, claims 3 and 41 have been amended to overcome the Office's rejections. Thus, claims 1, 13-15, 36-44, 60, and 61 satisfy the enablement requirement of 35 U.S.C. § 112.

35 U.S.C. § 103 Rejection

Reconsideration is requested of the rejection of claims 1, 13-15, 36-44, 60, and 61 as unpatentable under 35 U.S.C. § 103(a) over EP 0349453 (Martani) in view of U.S. Patent No. 5,846,990 (Murugesan) and Notenbomer (EP 0730494). Again, while Applicant believes the arguments presented in the response filed on August 20, 2008 are persuasive, to expedite prosecution, claim 1 has been amended so that is it directed to humans and incorporates the polymers of claim 16; the interview summary indicated these amendments would overcome this rejection. Thus, claims 1, 13-15, 36-44, 60, and 61 as patentable over EP 0349453 (Martani) in view of U.S. Patent No. 5,846,990 (Murugesan) and Notenbomer (EP 0730494) under 35 U.S.C. § 103(a).

Provisional Double Patenting Rejection

The analysis employed in an obvious-type double patenting rejection parallels the guidelines of a 35 U.S.C. § 103 obviousness determination.[1] However, an important distinction exists. A rejection for obviousness must be based on a comparison of the claimed invention to the entirety of the disclosure in the prior art reference, whereas an obviousness-type double patenting rejection must be grounded on a comparison of the claimed invention to the claims, **and only the claims**, of the reference.[2]

It is respectfully submitted that in light of the amendments made herein and the discussion of non-obviousness during the interview, the subject matter of the claims of the

[1] In re Braat, 937 F.2d 589 (Fed. Cir. 1991).
[2] Purdue Pharma L.P. v. Boehringer Ingelheim GMbH, 98 F.Supp.2d 362, 392, 55 USPQ2d 1168, 1190 (S.D.N.Y. 2000), *aff'd*, 237 F.3d 1359, 57 USPQ2d 1647 (Fed. Cir. 2001).

present application would not have been obvious in view of the claims of U.S. Patent No. 7,488,495 (U.S. Patent Application No. 10/965,274) or U.S. Patent Application No. 11/096,209. When evaluating the scope of a claim, every element of the claim must be considered.[3]

In particular, Applicants assert that a method of binding sodium is patentably distinct from a method of binding potassium. There are several distinct differences such that one of ordinary skill would not consider one obvious over the other under the obviousness-type double patenting standard articulated above. These differences include variances in (1) the relative and absolute amounts of sodium and potassium along the gastrointestinal tract; (2) the amounts of sodium and potassium depending upon the condition suffered by the patient; and (3) the selectivity of a cation exchange polymer for sodium and potassium ions.

The amount of sodium as compared to the amount of potassium available for binding will be different because the relative and absolute amounts of sodium and potassium in the gastrointestinal tract change depending on location (e.g., distance from the stomach). For example, Fordtran et al.,[4] who studied the sodium and potassium concentrations in the upper GI after different meals, (see especially Figs 2, 4 and 10), found that at the end of the ileum, the sodium concentration is relatively high, whereas the potassium concentration is relatively low. However, at the end of the gastrointestinal tract, the contents have a relatively high potassium concentration and a relatively low sodium concentration.[5]

Second, the pending claims of the instant application are directed to methods for removing sodium from a human in need thereof wherein the human is suffering from hypertension, chronic heart failure, end stage renal disease, liver cirrhosis, chronic renal insufficiency, fluid overload, or sodium overload. However, the '495 patent and the '209 application are directed to methods for removing potassium from a patient. When a subject suffers from hyperkalemia, the body compensates for the high intracellular potassium concentration in various ways, and thus, the amount of sodium or potassium found within the gastrointestinal tract in a hyperkalemic patient can be much different from the sodium and potassium concentrations of healthy people or patients suffering from the claimed diseases. For example, clinical evidence shows that hyperkalemic patients with renal dysfunction or chronic

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[3] See, e.g., In re Ochiai, 71 F.3d 1565, 1572, 37 USPQ2d 1127, 1133 (Fed. Cir. 1995).
[4] J.S. Fordtran et al. "Ionic Constituents and Osmolality of Gastric and Small-Intestinal Fluids after Eating," *Am. J. Digestive Dis.* **1966**, *11(7)*, 503. (submitted simultaneously in IDS).
[5] O. Wrong et al., "*In Vivo* Dialysis of Faeces as a Method of Stool Analysis," *Clin. Sci.* **1965**, *28*, 357-375. (see Figures 2 and 4); reference no. 6 submitted in IDS dated April 10, 2007.

kidney disease (CKD) who are not on dialysis increase potassium excretion in the terminal colon, as described in the review by Musso.[6] Specifically, Musso states:

> During CKD, the small intestine makes a greater contribution to potassium excretion than it does under normal conditions. Intestinal potassium excretion rises during chronic renal failure and the body can eliminate an additional 10–20 mmol of potassium by this route. Colonic potassium secretion begins to adapt when glomerular filtration is reduced to around one-third of normal and when renal failure is advanced, this route may account for as much as 30–70% of total potassium excretion.

This means that depending on the patient, the same cation-binding polymer can have a different effect on potassium and sodium concentrations in the body. Patients on drugs that affect potassium secretion, such as potassium sparing and non-potassium sparing diuretics, will have various perturbations in their sodium/potassium balance that may affect potassium and sodium availability in the gastrointestinal tract. Thus, these patients could also experience a different effect on potassium and sodium concentrations in the body upon administration of a cation-binding polymer.

Moreover, cation-binding polymers, generally, have a particular selectivity for certain cations over others – often reported as the selectivity coefficient. Generally, a cation-binding polymer selectively binds the counter ion of higher valence. The selectivity coefficient of a polymer within a particular class, however, can be modified by changing the crosslinking ratio or having a polyfunctional ion exchanger. Usually, decreasing the amount of crosslinker tends to decrease the potassium/sodium binding ratio (i.e. reduces the difference in their selectivity coefficients). Table 2 in the Dow Technical Information[7] shows that going from 16%DVB to 4% when crosslinking polystyrene sulfonate reduces the potassium:sodium selectivity coefficient ratio from 3.06/1.62 (i.e., 1.8) to 1.72/1.2 (i.e., 1.43).

A factor that reduces predictability is reversal of selectivity, which may be seen by at very high crosslinking ratios. This is generally described in Helfferich's book on ion exchange.[8] Table 5-10 shows that in sulfonated polystyrenes at 8 or 24% crosslinking, the preference for Na over Li or proton is significantly lower than predicted. In fact, there is an inversion seen for the

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[6] C.G. Musso, "Potassium Metabolism in Patients with Chronic Kidney Disease (CKD), Part I: Patients Not on Dialysis (Stages 3-4)," *International Urology and Nephrology* **2004**, *36*, 465-468. (submitted simultaneously in IDS)

[7] Form No. 177-01744-403XQRP. (simultaneously submitted in IDS).

[8] Helfferich, Ion Exchange, 1962, McGraw-Hill Book Company, Inc., pages 182-185. (simultaneously submitted in IDS).

Na selectivity coefficient at 24% crosslinking (3.06 predicted; 0.69 observed). Additionally, selectivity reversal can occur with polyfunctional ion exchangers (i.e. "resins containing different types of ionogenic groups").

In light of these technical differences, removing sodium from a particular patient population using a sodium-binding polymer would not have been obvious from methods for removing potassium from patients in need thereof. Thus, the methods are patentably distinct. In addition, particular reasons for withdrawing the current obviousness-type double patenting objections are as follows.

A. U.S. Patent Application No. 10/965,274

Reconsideration of the rejection of claims 1 and 36-44 as being unpatentable for nonstatutory obviousness-type double patenting over claims 1, 5, 8-17, and 30 of U.S. Patent Application No. 10/965,274 is respectfully requested. The '274 application is now US Patent 7,488,495, and claims 1, 5, 8-17, and 30 of the '274 were canceled. Nonetheless, it is respectfully submitted that the subject claims 1 and 36-40 are patentable in view of the '495 patent. The current claims are generally directed to methods for removing sodium from a patient suffering from hypertension, congestive heart failure, end stage renal disease, liver cirrhosis, chronic renal insufficiency, fluid overload, or sodium overload by administration of various cation exchange polymers. The '495 patent claims are directed to methods of treating hyperkalemia by administering cation-exchange polymers comprising an acid group having an electron-withdrawing group alpha or beta to an acid group and having a combination of counterions. Because the claims of the '495 patent do not include the element of removing sodium from a subject suffering from hypertension, congestive heart failure, end stage renal disease, liver cirrhosis, chronic renal insufficiency, fluid overload, or sodium overload, the claims do not include all the elements of instant claims 1 and 36-44. Further, since none of the sodium-binding polymers of instant claim 1 have an electron-withdrawing group attached to a carbon atom alpha or beta to the acid group, they would not have been obvious from the claims of the '495 patent requiring such polymers. Moreover, upon contemplation of the claims of the '495 patent, a person skilled in the art would not have found it obvious that the human subject of claim 1 herein suffered from hypertension, congestive heart failure, end stage renal disease, liver

cirrhosis, chronic renal insufficiency, fluid overload, or sodium overload. Thus, claims 1 and 36-44 are patentable over the claims of the '495 patent.

B. U.S. Patent Application No. 11/096,209

Reconsideration of the rejection of claims 1, 13-14, 36-43, 60, and 61 as being unpatentable for nonstatutory obviousness-type double patenting over claims 43-49, 52-59, and 61-64 of U.S. Patent Application No. 11/096,209 is respectfully requested. Subject claim 1 is directed to a method for removing sodium from a patient suffering from hypertension, congestive heart failure, end stage renal disease, liver cirrhosis, chronic renal insufficiency, fluid overload, or sodium overload by administration of various cation exchange polymers that do not specifically overlap with the polymers of the '209 application. Like the '495 patent, the claims[9] of the '209 application are generally directed to methods of removing potassium from the gastrointestinal tract of a mammal in need thereof by administering a specified crosslinked α-fluoroacrylic acid polymer, a crosslinked difluoromaleic acid polymer, or a salt thereof. Upon contemplation of the claims of the '209 application, a person skilled in the art would not have found it obvious that the human subject of instant claim 1 suffered from hypertension, congestive heart failure, end stage renal disease, liver cirrhosis, chronic renal insufficiency, fluid overload, or sodium overload. Thus, claims 1, 13-14, 36-43, 60, and 61 are patentable over the claims of the '209 application.

Rejoinder

Pursuant to MPEP §821.04, Applicants again request rejoinder of withdrawn claims 3, 5-11, 45-48, and 50-51 as they depend from claim 1, require all of the limitations of claim 1, and claim 1 is amended to include specific acid resin polymers. Furthermore, applicants submit that these claims are allowable over the references relied upon by the Office.

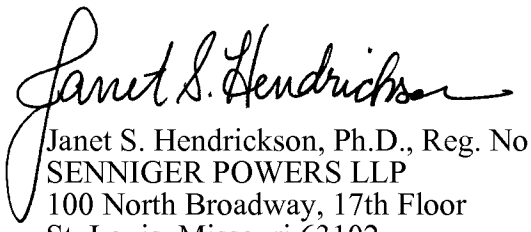
[9] It appears that the reference to claims 43-49, 52-59, and 61-64 of U.S. Patent Application No. 11/096,209 is incorrect.

CONCLUSION

Applicant submits that the present application is in condition for allowance and requests early allowance of the pending claims.

The Commissioner is hereby authorized to charge any under payment or credit any over payment to Deposit Account No. 19-1345.

Respectfully submitted,



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